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EXAMINER	
THANGAVELU, KANDASAMY	
ART UNIT	**PAPER NUMBER**
2123	

DATE MAILED: 11/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	09/878,686	SALE, MARK EDWARD	
	Examiner	Art Unit	
	Kandasamy Thangavelu	2123	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11 June 2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-26 of the application have been examined.

Domestic Priority not Granted

2. This application contains a claim for the benefit of priority based on U.S. Provisional Application No. 60/210,672 filed on June 10, 2000. Provisional Application 60/210,672 has been reviewed and priority granted.

Information Disclosure Statement

3. Acknowledgment is made of the information disclosure statements filed on June 11, 2001, with a list of patents and papers. The patents and papers have been considered in reviewing the claims.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications or other information submitted for consideration by the office, and MPEP § 609 A (1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Specifically, the specification makes references to various papers, patents and other publications on Pages 10-14 of the specification, but the documents have not been included in a proper Information

Disclosure statement. The applicants are requested to submit an IDS listing all the references, they wish considered. The applicants are also requested to send ***copies of all the non-patent references***, they wish to be considered

Drawings

4. The drawings submitted on June 11, 2001 are accepted.

Specification

5. The disclosure is objected to because of the following informalities:

Page 2, Lines 29-30, "occasionally, attempts are make to break the system of interest" appears to be incorrect and it appears that it should be "occasionally, attempts are made to break the system of interest

Page 5, Lines 3-4, "mass transfer rate constant out or compartment 1" appears to be incorrect and it appears that it should be "mass transfer rate constant out of compartment 1".

Page 8, Line 3, "the fourth model has two parameters to be estimates" appears to be incorrect and it appears that it should be "the fourth model has two parameters to be estimated".

Page 14, Line 20, "For example a parametergd either is …" appears to be incorrect and it appears that it should be "For example a parameter either is …".

Page 15, Lines 2-3, "each dimension represents a set of mutually excusive features from which exactly one is chosen for each candidate model". It is not understood as to what the applicant meant by "one is chosen". Is one dimension chosen or one set of mutually excusive features or one feature chosen?

Page 16, Lines 2-3, "each dimension represents a set of mutually excusive features from which exactly one is chosen for each candidate model". It is not understood as to what the applicant meant by "one is chosen". Is one dimension chosen or one set of mutually excusive features or one feature chosen?

Page 18, Lines 2-3, "each dimension represents a set of mutually excusive features from which exactly one is chosen for each candidate model". It is not understood as to what the applicant meant by "one is chosen". Is one dimension chosen or one set of mutually excusive features or one feature chosen?

Page 19, Lines 2-3, "each dimension represents a set of mutually excusive features from which exactly one is chosen for each candidate model". It is not understood as to what the applicant meant by "one is chosen". Is one dimension chosen or one set of mutually excusive features or one feature chosen?

Page 19, Lines 11-12, "each dimension represents a set of mutually excusive features from which exactly one is chosen for each candidate model". It is not understood as to what the applicant meant by "one is chosen". Is one dimension chosen or one set of mutually excusive features or one feature chosen?

Page 23, Lines 8-9, "If the matrix is diagonal ... then the diagonal elements are simply the inter subject variance" appears to be incorrect and it appears that it should

be "If the matrix is diagonal ... then the diagonal elements are simply the intra subject variance".

Page 25, Lines 15-16, "Genetic algorithm is chosen over other methods for a demonstration this invention for a number of reasons" appears to be incorrect and it appears that it should be "Genetic algorithm is chosen over other methods for a demonstration of this invention for a number of reasons".

Page 27, Line 18 to Page 28, Line 1, "Random effects in the model also be addressed are typically addressed " appears to be incorrect and it appears that it should be "Random effects in the model also to be addressed are typically addressed".

Page 28, Line 16, "all these attributed are typically required" appears to be incorrect and it appears that it should be "all these attributes are typically required".

Page 29, Lines 2-3, "twice the value of the standard error of estimate from some null value if the p value is to be $\prec 0.05$". What is p here?

Page 29, Lines 21-22, "the niche penalty will be a fraction ... of the difference between the most fit individual and the most fit individual that is not in the niche" appears to be incorrect and it appears that it should be "the niche penalty will be a fraction ... of the difference between the most fit individual in the niche and the most fit individual that is not in the niche".

Page 31, Lines 3-4, "the values between those loci are shifted left to right or right or left" appears to be incorrect and it appears that it should be "the values between those loci are shifted left to right or right to left".

Page 38, Lines 26-27, "This may be by change the value in one or more dimensions" appears to be incorrect and it appears that it should be "This may be by change of the value in one or more dimensions".

Page 39, Lines 6-7, "As T decreases, the probability of retaining a change that results in a worse model increases" appears to be incorrect and it appears that it should be "As T decreases, the probability of retaining a change that results in a worse model decreases".

Page 40, Lines 5-6, "commercially available (OptQuest . Boulder, CO." appears to be incorrect and it appears that it should be "commercially available (OptQuest . Boulder, CO).".

Appropriate corrections are required.

Claim Objections

6. The following is a quotation of 37 C.F.R § 1.75 (d)(1):

> The claim or claims must conform to the invention as set forth in the remainder of the specification and terms and phrases in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.

7. Claims 6 and 18 are objected to because of the following informalities:

Claim 6, "from which exactly is chosen for each candidate model and each model is represented by a bit string" appears to be incorrect and it appears that it should be

"from which exactly one is chosen for each candidate model and each model is represented by a bit string".

In Claim 18, "the presence of interinOdividual variability on each parameter" appears to be incorrect and it appears that it should be "the presence of interindividual variability on each parameter".

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4 and 6-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 states, "defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model". Independent claims 6, 17, 19, 21, 23 and 26 use similar language in the limitation. Claim 4 also uses the term, features.

The specification does not specify anywhere how the value of n, the dimensions of the model space is selected.

It does not describe **what a feature is,** that providing for wide interpretation by the examiner. Page 10, Lines 24-25, state "starting simple model and adding features to it"; so it is a component of the model. Page 11, Line 10 indicates that a feature is a term in the model. Page 10, Lines 24-25, state "starting simple model and adding features to it". Page 14, Lines 8-10, state "forward addition approach to model building ... when effects are added one at a time". So feature is an effect. But what is an effect? In Page 17, Lines 6-7 state, " sets of mutually exclusive features comprise one or more members of the group consisting of : .." and lists 27 items. Additionally, "the presence of interindividual variability on each parameter" could indicate as many items as there are parameters. Similarly, "the function describing the interindividual variability of each parameter", could mean many functions. . So this means that features are a large set of items, may be 50 or 100 or more. Some are parameters, some are logic values and some are functions and relationships. However, one of ordinary skill in the art could include shapes, sizes, colors, and textures etc as features depending on the field of his investigation. Without specific definition of the term "features", it is difficult to interpret the claims.

The specification does not indicate how mutually exclusive features are determined. In Page 17, Lines 6-7 state, " sets of mutually exclusive features comprise one or more members of the group consisting of : .." and lists 27 items. Additionally, "the presence of interindividual variability on each parameter" could indicate as many items as there are parameters. Similarly,

"the function describing the interindividual variability of each parameter", could mean many functions. . So this means that features are a large set of items, may be 50 or 100 or more; this is the group of features. Some are parameters, some are logic values and some are functions and relationships. How does one identify the sets of mutually exclusive features from this large set of items? What rules and procedures are used to identify the mutually exclusive features?

Claims rejected but not specifically addressed are rejected based on their dependency on rejected claims.

10. Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

10.1 Claim 1 states, "defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model". Independent claims 6, 17, 19, 21, 23 and 26 use similar language in the limitation.

The specification does not specify anywhere how the value of n, the dimensions of the model space is selected.

The specification does not indicate how mutually exclusive features are determined. In Page 17, Lines 6-7 state, " sets of mutually exclusive features comprise one or more members of

the group consisting of : .." and lists 27 items. Additionally, "the presence of interindividual variability on each parameter" could indicate as many items as there are parameters. Similarly, "the function describing the interindividual variability of each parameter", could mean many functions. . So this means that features are a large set of items, may be 50 or 100 or more; this is the group of features. Some are parameters, some are logic values and some are functions and relationships. How does one identify the sets of mutually exclusive features from this large set of items? What rules and procedures are used to identify the mutually exclusive features?

Claim 1 states, "defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model. What does "one is chosen for each candidate model" mean? Is a dimension or a set of features or a feature selected for each model?

Specification, Page 15, Lines 10-11, repeat what is stated in Claim 4. There it is stated that one feature from each of the n sets of candidate features is selected. How is this selection process done? By random choice or using any other criteria? There is no discussion of this selection process anywhere in the specification.

Assume for example that the group of features consists of 75 features. Say you can form 26 mutually exclusive sets of features, the sets being identified by A, B, C, ... to Z. Let the members of the sets be features (a1, a2, a3), (b1, b2), (c1 c2, c3, c4),... (z1, z2). So now we have placed the 75 features in 26 sets of mutually exclusive features. Suppose if one were to use a random process to select one feature from each set of mutually exclusive features, then models could be formed with 26 features in each one of them corresponding to 26 sets of features. If one were to select 100 models as candidate search space, the random process will result in selecting

all 75 of the features listed as part of the search space. Then what is achieved by grouping the features as sets of mutually exclusive features?

The specification shows one example of forming a search space on Page 35. Here sets of features are shown. Each set consisted of only one feature, a trivial example; each feature had multiple values that could be assigned to the feature. Therefore one of ordinary skill in the art will not know how to form the mutually exclusive sets of features from the group of features. He also will not know how to limit the selection process to 26 features when one feature from each set is selected at random and 75 features are in the 26 sets of features.

10.2 Claim 2 states, "the candidate search space is searched for a near optimal or optimal model". The claim does not state what criteria are used to select optimal or near optimal model. What is the objective function used?

10.3 Claim 3 states, "the search is accomplished by a method selected from the group consisting of: full grid search, simulated annealing, integer programming, scatter search/path relinking, neural networks, tabu search and genetic algorithm". The claim does not state how one goes about selecting one of these listed methods. What criteria are used to select one of the listed methods as the preferred method?

10.4 Claim 4 states, "selecting one feature from each of n sets of candidate features". The claim does not state how one of the features is selected from each set of features – by random method or using some other rule.

10.5 Claim 5 states, "A method for automated evaluation of the optimality of a model comprising: combining the log likelihood value with, optionally, a penalty for each parameter estimated, …". The claim does not state how automated evaluation of the optimality of a model is achieved by combining log likelihood value with various penalties. Determining optimality of model requires much more than combining log likelihood value with various penalties. It is a more complex iterative process.

10.6 Claim 6 states, "each model is represented by a bit string". Specification, Page 26, Line 21 to Page 27, Line 4 explain how each model is converted to a string. There, each feature is represented by 2 or more values. Some number of bits are assigned to each feature, so the value selected for the feature can be represented by the selected number of bits of that feature. The selection of the value for each feature can be at random. So by selecting the value for each feature in the model, a corresponding bit string for the model is achieved. It works alright if the features to be included in the model are preselected and remain constant.

However, the selection of features is done by "defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which exactly is chosen for each candidate model". Since one model is formed by selecting one feature from each set of mutually excusive features, in a system having 75 features and 26 mutually exclusive sets of features, the random selection of features for 100 models as an initial population, results in all the 75 features to be selected. Each model will have only 26 features. Therefore, it is necessary to indicate how the bits are assigned to all the 75

features. If all 75 features are represented in the bit string, then there will be bits assigned to (a1, a2, a3) of a mutually exclusive set A. When models are regenerated by cross over and mutation, it results in more than one feature from a set of mutually exclusive set of features appearing in the regenerated model; it also results in no feature from some sets of mutually exclusive sets of features appearing in the model. So what you end up with is random selection of features from the set of 75 features. Then what is achieved by grouping the features as sets of mutually exclusive features and initially selecting only one feature from each set of mutually exclusive features?

Claims rejected but not specifically addressed are rejected based on their dependency on rejected claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11.1. Claims 6-17, 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "assessing the fitness of each model in said population". There is insufficient antecedent basis for "said population" in this limitation.

Claim 7 recites the limitation "said initial population is a random population" in Line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 24 recites the limitation "The method of claim 23 wherein computer-readable code is configured to search the space for a near optimal or optimal model". There is insufficient antecedent basis for this limitation in the claim. Claim 23 refers to a computer program product and not a method.

Claim 25 recites the limitation "The method of claim 24 wherein the search is conducted using a method selected from the group…". There is insufficient antecedent basis for this limitation in the claim. The base claim 23 on which claim 24 depends refers to a computer program product and not a method.

12. Claims 1-3, 5 and 23-25 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

12.1 Claim 1 states, "A method for selecting a near optimal or optimal mathematical model from a set of candidate models, comprising:

defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model".

Defining a candidate search space having n dimensions and selecting one from each set of mutually exclusive features does not result in selecting a near optimal or optimal mathematical model from a set of candidate models. To select a near optimal or optimal mathematical model from a set of candidate models, it is essential to specify an objective function for optimization

and then search the models using the objective function and select the model with the optimum value of the objective function.

12.2 Claim 2 states, "the candidate search space is searched for a near optimal or optimal model". To search for a near optimal or optimal model from a set of candidate models, it is essential to specify an objective function for optimization and then search the models using the objective function. It is also necessary to select a procedure for searching the model space. What is the procedure is used to search the model space and how is that procedure selected?

12.3 Claim 3 states, "the search is accomplished by a method selected from the group consisting of: full grid search, simulated annealing, integer programming, scatter search/path relinking, neural networks, tabu search and genetic algorithm". Here the applicant has listed all the search techniques that he has come across from the literature. It is necessary to specify which one of these search techniques is selected and what is the criteria for selecting one search procedure over other.

12.4 Claim 5 states, "A method for automated evaluation of the optimality of a model comprising:

combining the log likelihood value with, optionally, a penalty for each parameter estimated...".

Combining the log likelihood value with, optionally, a penalty for each parameter estimated .., will only provide a new definition of log likelihood. That is not sufficient for automated evaluation of the optimality of a model. Additional steps are required.

12.5 Claims 23-25 are rejected based on the same reasoning as claims 1-3, since there are computer program product claims reciting the same limitations as claims 1-3.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 1-3, 6-20 and 23-26 are rejected under 35 U.S.C. 101 because the claimed inventions are directed to non-statutory subject matter.

14.1 Method claims 1-3 are rejected for reciting a process that is not directed to the technological arts.

Regarding claim 1, this claim is directed at a method for selecting a near optimal or optimal mathematical model from a set of candidate models, whereas none of the limitations describe any type of computer-implemented steps. To be statutory, the utility of an invention must be within the technological arts. *In re Musgrave*, 167 USPQ 280, 289-90 (CCPA, 1970). The definition of "technology" is the "application of science and engineering to the development

of machines and procedures in order to enhance or improve human conditions, or at least to improve human efficiency in some respect." (Computer Dictionary 384 (Microsoft Press, 2d ed. 1994)).

Dependent claims 2-3 depend on Claim 1 but do not add further statutory steps.

The limitations recited in claims 1-3 contain no language suggesting these claims are intended to be within the technological arts.

14.2 Method claims 6-16 are rejected for reciting a process that is not directed to the technological arts.

Regarding claim 6, this claim is directed at a method for selecting a near optimal or optimal mathematical model from a set of candidate models, whereas none of the limitations describe any type of computer-implemented steps. To be statutory, the utility of an invention must be within the technological arts, as explained in Paragraph 14.1 above.

Dependent claims 7-16 depend on Claim 6 but do not add further statutory steps.

The limitations recited in claims 6-16 contain no language suggesting these claims are intended to be within the technological arts.

14.3 Method claims 17-18 are rejected for reciting a process that is not directed to the technological arts.

Regarding claim 17, this claim is directed at a method for selecting a near optimal or optimal mathematical model from a set of candidate models, whereas none of the limitations describe any type of computer-implemented steps. To be statutory, the utility of an invention

must be within the technological arts, as explained in Paragraph 14.1 above.

Dependent claim 18 depends on Claim 17 but does not add further statutory steps.

The limitations recited in claims 17-18 contain no language suggesting these claims are intended to be within the technological arts.

14.4 Method claims 19-20 are rejected for reciting a process that is not directed to the technological arts.

Regarding claim 19, this claim is directed at a method for selecting a near optimal or optimal mathematical model from a set of candidate models, whereas none of the limitations describe any type of computer-implemented steps. To be statutory, the utility of an invention must be within the technological arts, as explained in Paragraph 14.1 above.

Dependent claim 20 depends on Claim 19 but do not add further statutory steps.

The limitations recited in claims 19-20 contain no language suggesting these claims are intended to be within the technological arts.

14.5 Independent claim 23 recites a computer program product comprising a computer usable storage medium having computer-readable program code embodied in the medium. The limitations recited in claim contain computer-readable code which is not statutory subject matter. To be statutory, the computer product should include a program comprising instructions which when executed in a computer performs a process comprising the steps included in the limitations.

The limitations recited in dependent claim 24 contain computer-readable code which is not statutory subject matter. Dependent claim 25 depends on Claim 24 but does not add further statutory steps.

14.6 Independent claim 26 recites a computer program product comprising a computer usable storage medium having computer-readable program code embodied in the medium. The limitations recited in claim contain computer-readable code which is not statutory subject matter. To be statutory, the computer product should include a program comprising instructions which when executed in a computer performs a process comprising the steps included in the limitations.

15.1 Claims 1- 3 would be statutory if claim 1 is written as a computer implemented method for selecting a near optimal or optimal mathematical model from a set of candidate models.

15.2 Claims 6- 16 would be statutory if claim 6 is written as a computer implemented method for selecting a near optimal or optimal mathematical model from a set of candidate models.

15.3 Claims 17- 18 would be statutory if claim 17 is written as a computer implemented method for selecting a near optimal or optimal mathematical model from a set of candidate models.

15.4 Claim 19- 20 would be statutory if claim 19 is written as a computer implemented method for selecting a near optimal or optimal mathematical model from a set of candidate models.

15. 5 Claim 23-25 would be statutory if claim 23 is rewritten as:

A computer program product comprising a computer usable storage medium having computer-readable instructions which when executed on a computer perform a process for selecting a near optimal or optimal mathematical model from a set of candidate models, the computer-readable instructions comprising:

15. 6 Claim 26 would be statutory if it is rewritten as:

A computer program product comprising a computer usable storage medium having computer-readable instructions which when executed on a computer perform a process for selecting a near optimal or optimal mathematical model from a set of candidate models, wherein the computer-readable instructions are configured to:

....

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

17. Claims 1-2 and 23-24 are rejected under 35 U.S.C. § 102(e) as being anticipated by **Cahill** (U.S. Patent Application 2002/0196975).

17.1 **Cahill** teaches population mixture modeling with an indeterminate number of sub-populations. Specifically, as per claim 1, **Cahill** teaches a method for selecting a near optimal or optimal mathematical model from a set of candidate models (Page 1, Para 0001, L2-3; Page 1, Para 0009, L3-6; Page 1, Para 0010, L1-6; Page 2, Para 0012, L1-14); comprising:

defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model (Page 2, Para 0012, L1-8; Page 2, Para 0013).

Per claim 2: **Cahill** teaches that the candidate search space is searched for a near optimal or optimal model (Page 1, Para 0010, L1-6; Page 2, Para 0012, L5-14; Page 2, Para 001; L8-12).

Per claim 23: **Cahill** teaches computer program product that selects a near optimal or optimal mathematical model from a set of candidate models, the computer program product comprising a computer usable storage medium having computer-readable program code embodied in the medium (Page 1, Para 0001, L2-3; Page 1, Para 0009, L3-6; Page 1, Para 0010,

L1-6; Page 2, Para 0012, L1-14; abstract, L1-2; Page 1, Para 0002); the computer-readable code comprising:

computer-readable code that is configured to accept a user defined candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which exactly one is chosen for each candidate model (Page 2, Para 0012, L1-8; Page 2, Para 0013; abstract, L1-2; Page 1, Para 0002).

Per claim 24: **Cahill** teaches that computer-readable code is configured to search the space for a near optimal or optimal model (Page 1, Para 0010, L1-6; Page 2, Para 0012, L5-14; Page 2, Para 001; L8-12; abstract, L1-2; Page 1, Para 0002).

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

19. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. Claims 3 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Cahill** (U.S. Patent Application 2002/0196975) in view of **Walser** (U.S. Patent 6,031,984), and further in view of **Rothberg et al.** (U.S. Patent 6,432,361), **Lee** (U.S. Patent 6,530,873), and **Phillips et al.** (U.S. Patent 6,792,399).

20.1 As per claim 3, **Cahill** teaches simulated annealing (Page 7, Para 0075, L11-13); and genetic algorithm (Page 2, Para 0013, L10-12; Page 7, Para 0071, L1-3).

Cahill does not expressly teach that the search is conducted using a method selected from the group consisting of: full grid search, simulated annealing, integer programming, scatter search/path relinking, neural network, tabu search and genetic algorithm. **Walser** teaches that the search is conducted using a method selected from the group consisting of: full grid search, simulated annealing, integer programming, scatter search/path relinking, neural network, tabu search and genetic algorithm (CL1, L60-62), because these methods form domain independent heuristic methods for many practically relevant combinatorial optimization problems (CL1, L58-61; CL1, L18-19). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Walser** that included the search being conducted using a method selected from the group consisting of: full grid search, simulated annealing, integer programming, scatter search/path relinking, neural network,

tabu search and genetic algorithm. The artisan would have been motivated because these methods would form domain independent heuristic methods for many practically relevant combinatorial optimization problems.

Cahill does not expressly teach full grid search. **Rothberg et al.** teaches full grid search (CL16, 26-28; CL18, L53-58), because the full search allows exhaustive search of all possible combinations to obtain the optimal model (CL16, 26-28; CL18, L53-58). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Rothberg et al.** that included full grid search. The artisan would have been motivated because the full search would allow exhaustive search of all possible combinations to obtain the optimal model.

Cahill does not expressly teach integer programming. **Lee** teaches integer programming (CL4, L21-24; CL4, L65 to CL5, L29; CL6, L22-35), because integer programming is an optimization method where the decision variables are restricted to be integers and the decision variables are constrained by a system of linear equations or inequities and the objective function to be optimized is expressed as a linear function of decision variables (CL5, L66 to CL6, L6). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included integer programming. The artisan would have been motivated because integer programming would be an optimization method where the decision variables were restricted to be integers and the decision variables were constrained by a system of linear equations or inequities and the objective function to be optimized was expressed as a linear function of decision variables.

Cahill does not expressly teach neural network. **Phillips et al.** teaches neural network (CL4, L33-40), because neural networks find blackboxes for forecasting using massive computerized databases and systems of mathematical equations; and the systems of empirically based equations have parameters that evolve over time and learn from the forecasting mistakes and self correct (CL4, L33-40). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Phillips et al.** that included neural network. The artisan would have been motivated because neural networks would find blackboxes for forecasting using massive computerized databases and systems of mathematical equations; and the systems of empirically based equations would have parameters that evolved over time and learnt from the forecasting mistakes and self corrected.

20.2 As per Claim 25, it is rejected based on the same reasoning as Claim 3, supra. Claim 25 is a computer program product claim reciting the same limitations as Claim 3, as taught throughout by **Cahill, Walser, Rothberg et al., Lee** and **Phillips et al.**

21. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Cahill** (U.S. Patent Application 2002/0196975) in view of **Thomas et al.** (U.S. Patent 5,857,462).

21.1 As per claim 5, **Cahill** teaches a method for automated evaluation of the optimality of a model (Page 1, Para 0010, L1-6; Page 2, Para 0012; Page 2, Para 0013, L8-12 and L23-26);

Cahill teaches likelihood value (Page 2, Para 0013, L2-5). **Cahill** does not expressly teach combining the log likelihood value with, optionally, a penalty for each parameter estimated, optionally, a penalty for each element of the interindividual variance matrix estimated, optionally, a penalty for each element of the intraindividual variance matrix estimated, optionally, a penalty imposed if the minimization does not conclude successfully, optionally, a penalty if the standard errors of the parameter estimates cannot be obtained, optionally, a penalty if the correlation matrix of the estimates has any element > 0.95, and optionally a "niche" penalty for being similar to other models in the population (within a "niche radius" of other models). **Thomas et al.** teaches combining the log likelihood value with, optionally, a penalty for each parameter estimated, optionally, a penalty for each element of the interindividual variance matrix estimated, optionally, a penalty for each element of the intraindividual variance matrix estimated, optionally, a penalty imposed if the minimization does not conclude successfully, optionally, a penalty if the standard errors of the parameter estimates cannot be obtained, optionally, a penalty if the correlation matrix of the estimates has any element > 0.95, and optionally a "niche" penalty for being similar to other models in the population (within a "niche radius" of other models) (Cl5, L50-59), because all these factors contribute to the fitness of the model (CL15, L59). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Thomas et al.** that included combining the log likelihood value with, optionally, a penalty for each parameter estimated, optionally, a penalty for each element of the interindividual variance matrix estimated, optionally, a penalty for each element of the intraindividual variance matrix estimated, optionally, a penalty imposed if the minimization does not conclude successfully, optionally, a penalty if the standard errors of the

parameter estimates cannot be obtained, optionally, a penalty if the correlation matrix of the estimates has any element > 0.95, and optionally a "niche" penalty for being similar to other models in the population (within a "niche radius" of other models). The artisan would have been motivated because all these factors contribute to the fitness of the model.

22. Claims 6-8, 11-12 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Cahill** (U.S. Patent Application 2002/0196975) in view of **Handa** (U.S. Patent 5,465,218), and further in view of **Lee** (U.S. Patent 6,530,873).

22.1 As per claim 6, **Cahill** teaches a method for selecting a near optimal or optimal mathematical model from a set of candidate models (Page 1, Para 0001, L2-3; Page 1, Para 0009, L3-6; Page 1, Para 0010, L1-6; Page 2, Para 0012, L1-14); comprising:

a) defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model (Page 2, Para 0012, L1-8; Page 2, Para 0013); and

each model is represented by a bit string (Fig. 3; Page 8, Para 0085, L9-12; Page 8, Para 0086; L1-3);

b) assessing the fitness of each model in the population (Page 2, Para 0013, L23-26).

Cahill does not expressly teach c) optionally, scaling the fitness of each model to be between and upper limit R and a lower limit S wherein the ratio of R to S is between 2:1 and 100:1. **Handa** teaches c) optionally, scaling the fitness of each model to be between and upper

limit R and a lower limit S wherein the ratio of R to S is between 2:1 and 100:1 (CL16, L44-50), because scaling prevents convergence on a local solution in a generation (CL26, L54-56). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Handa** that included c) optionally, scaling the fitness of each model to be between and upper limit R and a lower limit S wherein the ratio of R to S is between 2:1 and 100:1. The artisan would have been motivated because scaling would prevent convergence on a local solution in a generation.

Cahill teaches that individuals are selected for reproduction (Page 8, Para 0087, L13-14). **Cahill** does not expressly teach d) providing a number y of models to be in a subsequent generation. **Lee** teaches d) providing a number y of models to be in a subsequent generation (CL11, L1-2), because top scoring individuals are selected to parent offspring for the next generation (CL11, L32-34; CL11, L1-2). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included d) providing a number y of models to be in a subsequent generation. The artisan would have been motivated because top scoring individuals would be selected to parent offspring for the next generation.

Cahill teaches that individuals are selected for reproduction (Page 8, Para 0087, L13-14). **Cahill** does not expressly teach e) selecting with replacement y number of parents of the subsequent generation from the current generation. **Lee** teaches e) selecting with replacement y number of parents of the subsequent generation from the current generation (CL11, L36-37; CL11, L44-45), because subsequent generations will have same population as the previous generation (CL11, L34-35). It would have been obvious to one of ordinary skill in the art at the

time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included e) selecting with replacement y number of parents of the subsequent generation from the current generation. The artisan would have been motivated because subsequent generations would have same population as the previous generation.

Cahill teaches that the selection process evaluates the relative contribution of plurality of functions to the fitness (Page 2, Para 0013, L19-21). **Cahill** does not expressly teach that the probability of selection of a model in the current generation is proportional to the fitness or optionally to the scaled fitness. **Lee** teaches that the probability of selection of a model in the current generation is proportional to the fitness or optionally to the scaled fitness (CL11, L2-6), because that will select the individuals that are most fit and will optimize the objective function (CL11, L3-6). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included the probability of selection of a model in the current generation being proportional to the fitness or optionally to the scaled fitness. The artisan would have been motivated because that would select the individuals that would be most fit and would optimize the objective function.

Cahill teaches that individuals are selected for reproduction (Page 8, Para 0087, L13-14). **Cahill** does not expressly teach f) associating the parents into m groups comprising p parents where p is an integer greater than 1. **Lee** teaches f) associating the parents into m groups comprising p parents where p is an integer greater than 1 (CL11, L7-8), because that allows generating two new members for the next generation from each group, by interchanging subsections of two parents (CL11, L8-10). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of

Lee that included f) associating the parents into m groups comprising p parents where p is an integer greater than 1. The artisan would have been motivated because that would allow generating two new members for the next generation from each group, by interchanging subsections of two parents.

Cahill teaches that individuals are selected for reproduction and reproduction is simulated by cross over and mutation (Page 8, Para 0087, L13-15). **Cahill** does not expressly teach g) optionally, selecting some fraction of the m groups of parents to undergo at least one cross over. **Lee** teaches g) optionally, selecting some fraction of the m groups of parents to undergo at least one cross over (CL11, L35-37), because that that is analogous to cross over in biological reproduction, where a child's genetic composition is a combination of its parents (CL11, L10-12). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included g) optionally, selecting some fraction of the m groups of parents to undergo at least one cross over. The artisan would have been motivated because that that would be analogous to cross over in biological reproduction, where a child's genetic composition would be a combination of its parents.

Cahill teaches that individuals are selected for reproduction and reproduction is simulated by cross over and mutation (Page 8, Para 0087, L13-15). **Cahill** does not expressly teach h) optionally, crossing over the selected fraction at a random location on the bit string to create two new individuals for the subsequent generation. **Lee** teaches h) optionally, crossing over the selected fraction at a random location on the bit string to create two new individuals for the subsequent generation (CL11, L37-41), because that is analogous to cross over in biological

reproduction, where a child's genetic composition is a combination of its parents (CL11, L10-12). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included h) optionally, crossing over the selected fraction at a random location on the bit string to create two new individuals for the subsequent generation. The artisan would have been motivated because that that would be analogous to cross over in biological reproduction, where a child's genetic composition would be a combination of its parents.

Cahill teaches that individuals are selected for reproduction (Page 8, Para 0087, L13-14). **Cahill** does not expressly teach i) assigning bit strings in current generation that are not selected for cross over to the subsequent generation. **Lee** teaches i) assigning bit strings in current generation that are not selected for cross over to the subsequent generation (CL11, L34-37; CL11, L45-46), because to ensure the current best solution is not lost, the strategy of elitism is employed; so any individual not selected to be a parent is carried over (CL11, L51-54; CL11, L45-46). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included i) assigning bit strings in current generation that are not selected for cross over to the subsequent generation. The artisan would have been motivated because to ensure the current best solution is not lost, the strategy of elitism is employed; so any individual not selected to be a parent is carried over.

Cahill teaches that individuals are selected for reproduction and reproduction is simulated by cross over and mutation (Page 8, Para 0087, L13-15). **Cahill** does not expressly teach j) optionally, randomly mutate bits of the subsequent generation bit strings wherein the mutation comprises change a bit value 0 to a bit value of 1 or changing a bit value of 1 to a bit

value of 0. **Lee** teaches j) optionally, randomly mutate bits of the subsequent generation bit strings wherein the mutation comprises change a bit value 0 to a bit value of 1 or changing a bit value of 1 to a bit value of 0 (CL11, L42-47), because that is analogous to mutation in biological reproduction. It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included j) optionally, randomly mutate bits of the subsequent generation bit strings wherein the mutation comprises change a bit value 0 to a bit value of 1 or changing a bit value of 1 to a bit value of 0. The artisan would have been motivated because that would be analogous to mutation in biological reproduction.

Cahill teaches k) repeating the steps of b through j until the stopping criteria are met, where the stopping criteria are defined by the fitness function and is optimized to minimize the magnitude of the fit error (Page 2, Para 0012, L10-14; Page 2, Para 0013, L23-26; Page 8, Para 0087, L1-3). **Cahill** does not expressly teach k) repeating the steps of b through j until further improvement in mean and maximum fitness no longer occurs. **Lee** teaches k) repeating the steps of b through j until further improvement in mean and maximum fitness no longer occurs (CL11, L17-20), because then the difference between the maximum and minimum fitness values between the consecutive generations will be less than the specified threshold indicating near optimum value has been reached (CL11, L17-20). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included k) repeating the steps of b through j until further improvement in mean and maximum fitness no longer occurs 0. The artisan would have been motivated because then the difference between the maximum and minimum fitness values between the consecutive

generations would be less than the specified threshold indicating near optimum value had been reached.

22.2 As per claim 7, **Cahill, Handa** and **Lee** teach the method of claim 6. **Cahill** teaches that the initial population is a random population (Page 8, Para 0087, L6-7; Page 9, Para 0089, L3-6).

22.3 As per claim 8, **Cahill, Handa** and **Lee** teach the method of claim 6. **Cahill** teaches that the fitness is assessed by calculating some statistic of the goodness of fit of the model to the data (Page 2, Para 0012, L10-14; Page 2, Para 0013, L18-21).

Cahill does not expressly teach optionally, adding cost associated with desirable attributes of the model, including parsimony (fewer parameters). **Handa** teaches optionally, adding cost associated with desirable attributes of the model, including parsimony (fewer parameters) (CL22, L36-40), because the smaller the cost, the better the solution is (CL22, L36). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Handa** that included optionally, adding cost associated with desirable attributes of the model, including parsimony (fewer parameters). The artisan would have been motivated because the smaller the cost, the better the solution would be.

22.4 As per claim 11, **Cahill, Handa** and **Lee** teach the method of claim 6. **Cahill** teaches that individuals are selected for reproduction (Page 8, Para 0087, L13-14). **Cahill** does not expressly teach that the number of models in the subsequent generation is equal to the number of

models in the current generation. **Lee** teaches that the number of models in the subsequent generation is equal to the number of models in the current generation (CL11, L32-35), because top scoring individuals are selected to parent offspring for the next generation (CL11, L32-34; CL11, L1-2). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included the number of models in the subsequent generation being equal to the number of models in the current generation. The artisan would have been motivated because top scoring individuals would be selected to parent offspring for the next generation.

22.5 As per claim 12, **Cahill, Handa** and **Lee** teach the method of claim 6. **Cahill** teaches that individuals are selected for reproduction (Page 8, Para 0087, L13-14). **Cahill** does not expressly teach that the number of parents in each group, p = 2. **Lee** teaches that the number of parents in each group, p = 2 (CL11, L7-8), because two parents are required for effecting cross over as in biological systems so new members of next generation can be formed (CL11, L7-11). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Lee** that included the number of parents in each group, p = 2. The artisan would have been motivated because two parents would be required for effecting cross over as in biological systems so new members of next generation could be formed.

22.6 As per Claim 26, it is rejected based on the same reasoning as Claim 6, supra. Claim 26 is a computer program product claim reciting the same limitations as Claim 6, as taught throughout by **Cahill, Handa** and **Lee.**

23. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Cahill** (U.S. Patent Application 2002/0196975) in view of **Handa** (U.S. Patent 5,465,218), and further in view of **Lee** (U.S. Patent 6,530,873) and **Hottinen et al.** (U.S. Patent 6,449,266).

23.1 As per claim 9, **Cahill, Handa** and **Lee** teach the method of claim 8. **Cahill** teaches the goodness of fit of the model to the data (Page 2, Para 0013, L23-26) and the likelihood of the misclassification of the data (Page 2, Para 0013, L4-7).

Cahill does not expressly teach that the goodness of fit of the model to the data is the log likelihood of the data, given the model. **Hottinen et al.** teaches that the goodness of fit of the model to the data is the log likelihood of the data, given the model (CL7, L34-35), because the log likelihood can be used as optimality criterion (CL7, L31-35). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Hottinen et al.** that included the goodness of fit of the model to the data being the log likelihood of the data, given the model. The artisan would have been motivated because the log likelihood could be used as optimality criterion.

24. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Cahill** (U.S. Patent Application 2002/0196975) in view of **Handa** (U.S. Patent 5,465,218), and further in view of **Lee** (U.S. Patent 6,530,873), **Griffith et al.** (U.S. Patent 6,197,575) and **Reznik et al.** (U.S. Patent 6,368,813).

24.1 As per claim 15, **Cahill, Handa** and **Lee** teach the method of claim 6. **Cahill** does not expressly teach that the models represent pharmacokinetic models or pharmacodynamic models. **Griffith et al.** teaches pharmacokinetic models or pharmacodynamic models (CL1, L13-18; CL4, L29-33), because that allows determining the effects of biological and/or chemical agents on the tissue arrays (CL1, L14-17). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Griffith et al.** that included pharmacokinetic models or pharmacodynamic models. The artisan would have been motivated because that would allow determining the effects of biological and/or chemical agents on the tissue arrays.

Cahill does not expressly teach that the models represent pharmacokinetic models or pharmacodynamic models. **Reznik et al.** teaches that the models represent pharmacokinetic models or pharmacodynamic models (CL2, L51-53; CL12, L28-32), because as per **Lee** a genetic algorithm is a heuristic method modeled on biological mechanisms of evolution and natural selection (CL10, L56-58). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Reznik et al.** that included the models represent pharmacokinetic models or pharmacodynamic models.

The artisan would have been motivated because a genetic algorithm is a heuristic method modeled on biological mechanisms of evolution and natural selection.

25. Claims 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Cahill** (U.S. Patent Application 2002/0196975) in view of **Rothberg et al.** (U.S. Patent 6,432,361).

25.1 As per claim 17, **Cahill** teaches a method for selecting a near optimal or optimal mathematical model from a set of candidate models (Page 1, Para 0001, L2-3; Page 1, Para 0009, L3-6; Page 1, Para 0010, L1-6; Page 2, Para 0012, L1-14); comprising:

defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model (Page 2, Para 0012, L1-8; Page 2, Para 0013).

Cahill teaches simulated annealing (Page 7, Para 0075, L11-13). **Cahill** does not expressly teach that simulated annealing comprises the steps of:

i) randomly selecting one model from the candidate search space;

ii) selecting an initial value for temperature (T) wherein T represents the tolerance of a minimization process for retaining a change in the model that results in a higher energy;

iii) assessing the energy of the initial model;

iv) randomly changing the model to generate a subsequent model;

v) assessing the energy of the subsequent model;

vi) retaining the subsequent model as the current model if the energy is lower than the current model;

vii) if the energy of the subsequent model is higher than the energy of the current model the probability of retaining it is equal to:

$$e^{\Delta E/KT}$$

where T is the temperature, ΔE is the change in energy (current model energy - subsequent model energy), and k is Boltzmans constants; or

Otherwise, rejecting the subsequent model;

viii) reducing the value of T; and

ix) repeating the steps of iv through viii until further reduction in energy no longer occurs.

Rothberg et al. teaches that simulated annealing comprises the steps of:

i) randomly selecting one model from the candidate search space (Fig 13A, Step 1702; CL67, L54-57; CL68, L11-12);

ii) selecting an initial value for temperature (T) wherein T represents the tolerance of a minimization process for retaining a change in the model that results in a higher energy (Fig 13A, Step 1702; CL67, L53-54; CL68, L10-11);

iii) assessing the energy of the initial model (Fig 13A, Step 1703; CL67, L6-10; CL68, L17-20);

iv) randomly changing the model to generate a subsequent model (Fig 13A, Step 1707; CL68, L26-28);

v) assessing the energy of the subsequent model (Fig 13A, Step 1708; CL68, L28-30);

vi) retaining the subsequent model as the current model if the energy is lower than the current model (Fig 13A, Step 1711; CL68, L30-33);

vii) if the energy of the subsequent model is higher than the energy of the current model the probability of retaining it is equal to:

$$e^{\Delta E/KT}$$

where T is the temperature, ΔE is the change in energy (current model energy - subsequent model energy), and k is Boltzmans constants (Fig 13A, Step 1710; CL67, L47-48; CL68, L33-42); or

Otherwise, rejecting the subsequent model (CL68, L42-43);

viii) reducing the value of T (Fig 13A, Step 1712; CL67, L58-60; CL67, L9-12; CL68, L50-52); and

ix) repeating the steps of iv through viii until further reduction in energy no longer occurs (Fig 13A, Step 1712 to Step 1703; CL68, L50-52).

It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Rothberg et al.** that included all the implementation steps for simulated annealing. The artisan would have been motivated because **Rothberg et al.** provides all the implementation steps for simulated annealing.

25.2 As per claim 19, **Cahill** teaches a method for selecting a near optimal or optimal mathematical model from a set of candidate models (Page 1, Para 0001, L2-3; Page 1, Para 0009, L3-6; Page 1, Para 0010, L1-6; Page 2, Para 0012, L1-14); comprising:

defining a candidate search space having n dimensions, wherein n is a positive integer and each dimension represents a set of mutually exclusive features from which one is chosen for each candidate model (Page 2, Para 0012, L1-8; Page 2, Para 0013).

Cahill does not expressly teach b) searching the candidate search space using full grid search wherein full grid comprises the evaluation of every possible model in the search space. **Rothberg et al.** teaches b) searching the candidate search space using full grid search wherein full grid comprises the evaluation of every possible model in the search space (CL16, 26-28; CL18, L53-58), because the full search allows exhaustive search of all possible combinations to obtain the optimal model (CL16, 26-28; CL18, L53-58). It would have been obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of **Cahill** with the method of **Rothberg et al.** that included b) searching the candidate search space using full grid search wherein full grid comprises the evaluation of every possible model in the search space. The artisan would have been motivated because the full search would allow exhaustive search of all possible combinations to obtain the optimal model.

Conclusion

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Kandasamy Thangavelu whose telephone number is 571-272-3717. The examiner can normally be reached on Monday through Friday from 8:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kevin Teska, can be reached on 571-272-3716. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-9600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

K. Thangavelu
Art Unit 2123
November 9, 2004

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